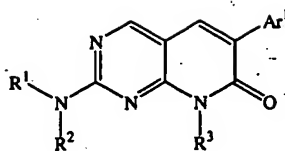


WHAT IS CLAIMED IS:

1. A compound of the formula:



5

a prodrug or a salt thereof,

wherein:

$R^1$  is hydrogen or alkyl;

- 10  $R^2$  is  $-CR'R''-R^a$  (where  $R'$  and  $R''$  are hydrogen, hydroxyalkyl or alkyl with at least one being alkyl or hydroxyalkyl and  $R^a$  is hydroxyalkyl),  $R^x-S-R^y$  (where  $R^x$  is alkyl and  $R^y$  is alkylene), alkoxy-substituted alkyl, heterocyclalkyl or  $C_4-C_5$  cycloalkyl, wherein each of the hydroxy group present in  $R^2$  can be independently in the form of an ester, a carbamate, a carbonate, or a sulfonate derivative; or

- 15  $R^1$  and  $R^2$  together with the nitrogen atom to which they are attached form a heterocycl group;

$R^3$  is hydrogen, alkyl, amino, monoalkylamino, dialkylamino, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene- $C(O)-R$  (where  $R$  is hydrogen, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino) or acyl; and

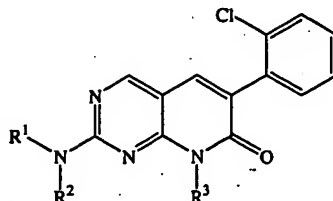
$Ar^1$  is aryl.

- 20 2. The compound of Claim 1 wherein  $Ar^1$  is an optionally substituted phenyl.

3. The compound of Claim 2, wherein  $Ar^1$  is a phenyl group independently substituted with one or two halo, alkyl or methoxy groups.

4. The compound of Claim 3, wherein  $Ar^1$  is 2-chlorophenyl, 2-methylphenyl or 2-methoxyphenyl.

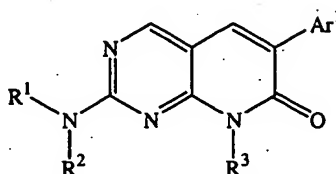
5. The compound according to claim 4 of the formula:



6. The compound according to claim 5, wherein R<sup>1</sup> is hydrogen or methyl.

7. The compound according to claim 6, wherein R<sup>2</sup> is (1,1-dimethyl-2-hydroxy)ethyl, (1,2-dimethyl-2-hydroxy)propyl, or (1-substituted piperidin-4-yl)methyl, wherein each of the hydroxy group present in R<sup>2</sup> can be independently in the form of an ester, a carbamate, a carbonate, or a sulfonate derivative.

8. A composition comprising:  
 (a) an excipient; and  
 (b) a compound of the formula:



a prodrug or a pharmaceutically acceptable salt thereof,

wherein

R<sup>1</sup> is hydrogen or alkyl;

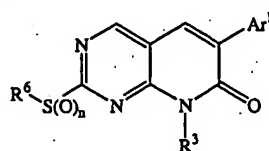
R<sup>2</sup> is -CR'R''-R<sup>a</sup> (where R' and R'' are hydrogen, hydroxyalkyl or alkyl with at least one being alkyl or hydroxyalkyl and R<sup>a</sup> is hydroxyalkyl), R<sup>x</sup>-S-R<sup>y</sup>- (where R<sup>x</sup> is alkyl and R<sup>y</sup> is alkylene), alkoxy-substituted alkyl, heterocyclalkyl or C<sub>4</sub>-C<sub>5</sub> cycloalkyl, wherein each of the hydroxy group present in R<sup>2</sup> can be independently in the form of an ester, a carbamate, a carbonate, or a sulfonate derivative; or

R<sup>1</sup> and R<sup>2</sup> together with the nitrogen atom to which they are attached form a heterocycl group;

$R^3$  is hydrogen, alkyl, amino, monoalkylamino, dialkylamino, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene-C(O)-R (where R is hydrogen, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino) or acyl; and

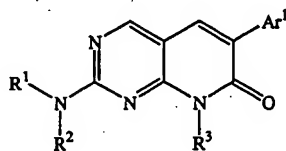
$Ar^1$  is aryl.

- 5            9.        A method for preparing a compound of Claim 1, comprising the steps of contacting a compound of the formula Ig:



Ig

- 10        with an amine of the formula  $R^1R^2NH$  under conditions sufficient to produce a compound of Formula I:



wherein:

$R^1$ ,  $R^2$ ,  $R^3$  and  $Ar^1$  are those defined in claim 1;

L is a leaving group;

- 15        n is an integer from 0 to 2; and

$R^6$  is an alkyl group.

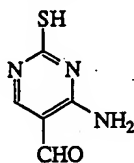
10.        The method of claim 9, wherein n is 1.

11.        The method of claim 9 wherein n is 2.

12.        A method for treating a p38 mediated disorder comprising administering to a patient in need of such treatment, an effective amount of a compound of Claim 1.

13.        The method of claim 12, wherein said p38 mediated disorder is arthritis, Crohns disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome or chronic obstructive pulmonary disease.

14. A process for producing a pyrimidine of the formula:



II-c

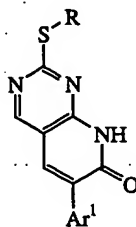
comprising:

- 5 (a) contacting an acetal of the formula  $\text{NC}-\text{CH}_2-\text{C}(\text{OR}^a)_2$ , with an alkyl formate of the formula  $\text{HCO}_2\text{R}$  in the presence of a condensation base under conditions sufficient to produce a condensed product; and
- (b) contacting said condensed product with thiourea in the presence of a cyclization base under conditions sufficient to produce said pyrimidine of Formula II-c,
- 10 wherein each of R and  $\text{R}^a$  is independently alkyl.

15. The process of Claim 14, wherein said condensation base is a tert-butoxide.

16. The process of Claim 14, wherein said cyclization base is an alkoxide.

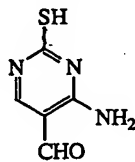
17. A process for producing a pyridopyrimidine of the formula:



II-e

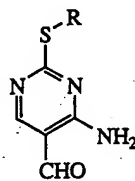
comprising:

- (a) contacting a pyrimidine of the formula:



II-c

with an alkylating agent of the formula  $R-X^1$  in the presence of an alkylating base under conditions sufficient to produce an alkylated pyrimidine of the formula:



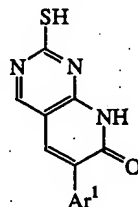
**II-d**

and

(b) contacting said alkylated pyrimidine of Formula **II-d** with an aryl acetate of the formula  $Ar^1-CH_2-CO_2R$  in the presence of a cyclization base under conditions sufficient to produce said pyridopyrimidine of Formula **II-e**

or

(a) contacting said pyrimidine of Formula **II-c** with said aryl acetate of the formula  $Ar^1-CH_2-CO_2R$  in the presence of a cyclization base under conditions sufficient to produce a thiol pyridopyrimidine of the formula:



**III**

and

(b) contacting said thiol pyridopyrimidine of Formula **III** with said alkylating agent of the formula  $R-X^1$  in the presence of an alkylating base under conditions sufficient to produce said pyridopyrimidine of Formula **II**,

wherein

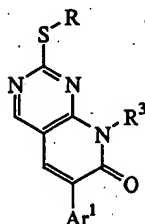
$X^1$  is a leaving group;

each R is independently alkyl;

$Ar^1$  is aryl;

18. The process of Claim 17, wherein  $X^1$  is halide.

19. The process of Claim 17 further comprising contacting said pyridopyrimidine of Formula II with a nitrogen alkylating agent of the formula  $R^3-X^2$  under conditions sufficient to produce an N-substituted pyridopyrimidine of the formula:



wherein

$R^3$  is alkyl, amino, monoalkylamino, dialkylamino, cycloalkyl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene- $C(O)-R'$  (where  $R'$  is hydrogen, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino) or acyl;

$X^2$  is a leaving group; and

$Ar^1$  and  $R$  are those defined in Claim 17.

20. The process of Claim 19, wherein  $X^2$  is a halogen.

\* \* \* \* \*